REMARKS

Status of the Claims

Claims 17-55 are pending. Claims 17-24, 31-39 and 41-55 are withdrawn from consideration as being drawn to a non-elected invention. Claims 25-30 and 40 are rejected. Claims 26-27, 29, 30 and 40 are cancelled. Claims 25 and 28 are amended. No new matter has been added. Reconsideration of the pending claims is respectfully requested.

Amendments to the claims

Claims 26-27, 29, 30 and 40 are cancelled. Claims 25 and 28 are amended to overcome the rejections under 35 U.S.C. 112, first paragraph. No new matter has been added.

Application Data Sheet/Specification

The Application Data Sheet and Specification are objected to because of the following informality: the Domestic Priority Information needs to be updated to properly identify that the Application is a Continuation of 09/484,903 filed on January 18, 2000, now U.S. Patent 4,448,086.

The Application Data Sheet and Specification are amended to identify that the Application is a Continuation of application Serial No. 09/484,903, filed on January 18, 2000, now U.S. Patent No. 6,448,086. Reconsideration is therefore respectfully requested.

Claim objections

Claims 26, 27 and 29 are objected to as being drawn to non-elected inventions. The objection to claims 26, 27, and 29 is moot, because these claims have been cancelled. Reconsideration is therefore respectfully requested.

The 35 U.S.C. 112, first paragraph rejections

Claims 25-30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art to make and use the invention commensurate in scope with the claims.

The Examiner states that the specification, while being enabling for a method of discriminating between benign prostate disorders and prostate cancer by calculating a ratio based on at least two of the measured concentrations of either IGF-I, IGFBP-3, and PSA does not reasonably provide enablement for providing a means for discriminating between any and/or all benign disorders and cancers by calculating a ratio based on at least two of the measured concentrations of either IGF-I, IGFBP-3, and PSA.

Applicants respectfully traverse the Examiner's rejection. Claim 25 has been amended to recite a diagnostic method for discriminating between benign prostate disorders and prostate cancer in an individual by calculating a ratio based on at least two of the measured concentrations of IGF-I, IGFBP-3, and PSA. Claim 28 is dependent on claim 25 and is amended to further recite that IGFBP-3 is total or intact IGFBP-3.

Accordingly, Applicants respectfully argue that claims 25 and 28 as amended are enabled under 35 USC 112, first paragraph.

The rejection of claims 26-27 and 29-30 is moot, because claims 26-27 and 29-30 have been cancelled.

Accordingly, Applicants respectfully request that the rejections of claims 25-30 under 35 U.S.C. 112, first paragraph, be withdrawn.

The 35 U.S.C. §102 rejections

Claims 25-30 and 40 are rejected under 35 U.S.C. 102(e) as being anticipated by Pollak *et al.* (U.S. 6,645,770, 1998). Applicants respectfully traverse this rejection.

The Examiner states that Pollak discloses methods of assessing the risk of developing prostate cancer in an individual, involving measuring IGF-I and/or IGFBP-3 in a specimen from the individual, where high levels of IGF and/or low levels of IGFBP correlate with increased risk of developing prostate cancer. In addition, Pollak teaches a method to determine the IGF/PSA status of an individual by combining the IGF status with a measurement of PSA levels. Further, in addition to predicting prostate cancer Pollak teaches that the method can be useful in differentiating cancer from other prostatic diseases, such as benign prostatic hyperplasia. Finally, Pollak teaches that total, complexed or free IGFBP-3 may be measured. The claims are drawn to a diagnostic method for discriminating between benign disorders and cancer, by measuring the concentrations of an IGFBP such as IGFBP-3, and growth factor such as IGF-I, and a tumor marker concentration such as PSA in a body fluid from an individual, and calculating an indicator ratio based on at least two of the measured concentrations, where

the ratio provides a means for discriminating between benign disorders and cancer. Therefore, the claims are anticipated by Pollak.

Applicants respectfully traverse the Examiner's rejection. First, Pollak teaches methods to predict the risk of developing prostate cancer in the future, by determining the IGF status in the individual before the onset of prostate cancer. The subjects in the Pollak study had no history of cancer, except for non-melanoma skin cancer (column 6, lines 19-23). High levels of IGF and/or low levels of IGFBP were correlated with increased risk of eventually developing prostate cancer (column 1, lines 30-32, Tables 1 and 2). Additionally, Pollak teaches that men having PSA levels above 4 ng/ml are more likely to be subsequently diagnosed with prostate cancer, and that higher IGF-I levels (adjusted for IGFBP-3) have a strong relation to risk of developing prostate cancer in men with a baseline PSA of less than 4 ng/ml that becomes stronger in men with PSA levels higher than 4 ng/ml (column 11, lines 10-26, and Table 3). Pollak accordingly suggests that measurements of IGF-I levels in addition to PSA may better predict subsequent prostate cancer than PSA measurements alone (column 11, lines 26-31). Thus, these teachings of Pollak are to use IGF-I, IGFBP-3 and PSA measurements in subjects without any evidence of prostate disease, to predict the risk of occurrence of prostate cancer in the future.

In contrast, the present claims describe methods to discriminate between benign prostate disorders and prostate cancer in an individual already having such a disorder or cancer, by calculating an indicator ratio based on at least two of the measured concentrations of either IGF-I, IGFBP-3, and PSA in a sample from that individual. The teachings of Pollak only provide methods to predict the future development of prostate

cancer, and not to discriminate between a benign prostate disorder and prostate cancer; therefore, the teachings of Pollak do not anticipate the present claims.

Second, defining "prostate disease" as inclusive of prostate cancer and benign prostatic hyperplasia, Pollak states that the methods described therein are most preferably used to determine the risk of an individual developing prostate cancer, diagnosing prostate cancer, or assessing the progress of the cancer; and that accordingly, the described methods may be useful in predicting prostate cancer, differentiating cancer from other prostatic diseases (column 5, lines 8-18). Pollak does teach methods to predict the future onset of prostate cancer in an individual without prostate cancer, but does not teach that these methods can be used to diagnose existing prostate cancer, or discriminate between existing prostate cancer and a benign prostate disorder. Indeed, Pollak indicates that in one particular study IGF-I levels were only of "borderline significance" in predicting prostate cancer risk in men already diagnosed with prostate cancer, and that the retrospective design used in the study could not rule out an effect of the cancer, or treatment, on IGF-I levels (column 12, lines 6-20). None of the teachings of Pollak demonstrates any utility of the methods described to diagnose existing prostate cancer or a benign prostate disease, or to discriminate between existing prostate cancer and a benign prostate disorder.

In addition, Pollak states that the IGF/PSA status provides an improved method of assessing the prognosis of existing prostate cancer (column 1, lines 36-38), and that high IGF and PSA levels or low IGFBP levels are indicative of individuals at risk for severe prostate cancer or who have prostate cancer with a poor prognosis (column 4, lines 47-51). As described above, Pollak teaches that high IGF-I levels combined with high PSA

levels correlate to a higher risk of eventually developing prostate cancer. The teachings of Pollak are therefore confined to the prediction of prostate cancer as opposed to other prostatic diseases. At best, by providing a method to predict prostate cancer in the future, Pollak might provide a method to predict the risk of developing prostate cancer in the future, as opposed to the risk of developing a benign prostate disease in the future.

In order for an applicant's invention to be anticipated by a prior art disclosure under section 102, the reference must contain an "enabling disclosure" (M.P.E.P. 2121.01). The disclosure is enabling if the public was in possession of the claimed invention before the date of invention, "possession" being effected if one of ordinary skill in the art could have combined the reference's description of the invention with his/her own knowledge to make the claimed invention (*Id.*). Pollak states that "no one has heretofore shown that markers relating to IGF-axis components can also be used as a risk marker for prostate cancer (column 2, line 67-column 3, lines 1-3). The teachings of Pollak only show that IGF axis measurements can be used to predict the risk of future prostate cancer. Therefore, the teachings of Pollak do not provide an enabling disclosure that anticipates the presently claimed invention.

The rejection of claims 26-27, 29, 30 and 40 is moot, because these claims are cancelled.

Accordingly, Applicants respectfully request that the rejection of claims 25-30 and 40 under 35 U.S.C. 102(e) be withdrawn.

Double Patenting rejection

Claims 25-30 and 40 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2 and 4 of U.S. Patent No. 6,448,086.

The rejection of claims 26-27, 29, 30 and 40 is moot, because these claims are cancelled. Regarding claims 25 and 28, Applicants respectfully refer the Examiner to the enclosed Terminal Disclaimer. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome a rejection based on nonstatutory double patenting, if the conflicting application or patent is shown to be commonly owned with this application. Accordingly, Applicants respectfully request that the rejection of claims 25-30 and 40 under the judicially created doctrine of obviousness-type double patenting be withdrawn.

This is intended to be a complete response to the Office Action mailed January 13, 2005. If any issues remain outstanding, the Examiner is respectfully requested to contact the undersigned for immediate resolution.

Respectfully submitted,

Date: May 12, 2005

Holly O. Soehnge, Ph.D., J.D.
Registration No. 54,786
Agent for Applicant

Diagnostic Systems Laboratories, Inc.
445 Medical Center Boulevard
Webster, TX 77598-4217
(281) 332-9678 ext. 1205
hsoehnge@dslabs.com